

What Is Claimed Is:

1. An article of manufacture comprising packaging material and a pharmaceutical agent contained within said packaging material, wherein said pharmaceutical agent is effective for inhibiting angiogenesis in a tissue and wherein said packaging material comprises a label which indicates that said pharmaceutical agent can be used for treating conditions by inhibition of angiogenesis and wherein said pharmaceutical agent comprises an angiogenesis-inhibiting amount of an $\alpha_v\beta_3$ antagonist that comprises a polypeptide having an amino acid residue sequence that includes a portion of the carboxy terminal domain of matrix metalloproteinase, said polypeptide capable of binding to integrin $\alpha_v\beta_3$.
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- 10 2. The article of manufacture of claim 1 wherein said polypeptide includes an amino acid residue sequence shown in SEQ ID NO 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22.
3. The article of manufacture of claim 1 wherein said tissue is inflamed and said condition is arthritis or rheumatoid arthritis.
- 15 4. The article of manufacture of claim 1 wherein said tissue is a solid tumor or solid tumor metastasis.
5. The article of manufacture of claim 1 wherein said tissue is retinal tissue and said condition is retinopathy, diabetic retinopathy or macular degeneration.
- 20 6. An $\alpha_v\beta_3$ antagonist comprising a polypeptide having an amino acid residue sequence that includes a portion of the carboxy terminal domain of matrix metalloproteinase, said polypeptide capable of binding to integrin $\alpha_v\beta_3$.
7. The antagonist of claim 6 wherein said polypeptide includes an amino acid residue sequence shown in SEQ ID NO 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22.
8. The antagonist of claim 6 wherein said polypeptide is a fusion protein.
9. The antagonist of claim 6 wherein said polypeptide has an amino acid residue sequence shown in SEQ ID NO 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22.
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10. A pharmaceutical agent comprising an $\alpha_v\beta_3$ antagonist according to claim 6 in a pharmaceutically acceptable carrier in an amount sufficient to inhibit angiogenesis in a tissue.
11. A method for inhibiting angiogenesis in a tissue comprising administering to said tissue a composition comprising an angiogenesis-inhibiting amount of an $\alpha_v\beta_3$ antagonist.
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12. The method of claim 11 wherein said antagonist is a fusion protein, a polypeptide, a derivatized polypeptide, a cyclic polypeptide, a monoclonal antibody or an organic mimetic compound.
13. The method of claim 11 wherein said integrin $\alpha_v\beta_3$, antagonist preferentially inhibits fibrinogen binding to $\alpha_v\beta_3$ compared to fibrinogen binding to $\alpha_{IIb}\beta_3$.

14. The method of claim 11 wherein said $\alpha_v\beta_5$ antagonist comprises a polypeptide having an amino acid residue sequence that includes a portion of the carboxy terminal domain of matrix metalloproteinase, said polypeptide capable of binding to integrin $\alpha_v\beta_5$.

15. The method of claim 11 wherein said polypeptide includes an amino acid residue sequence shown in SEQ ID NO 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22.

16. The method of claim 11 wherein said polypeptide is a fusion protein.

17. The method of claim 11 wherein said polypeptide has an amino acid residue sequence shown in SEQ ID NO 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22.

18. The method of claim 11 wherein said tissue is inflamed and said angiogenesis is inflamed tissue angiogenesis.

19. The method of claim 18 wherein said tissue is arthritic.

20. The method of claim 19 wherein said arthritic tissue is present in a mammal with rheumatoid arthritis.

21. The method of claim 11 wherein said tissue is the retinal tissue of a patient with diabetic retinopathy and said angiogenesis is retinal angiogenesis.

22. The method of claim 11 wherein said tissue is a solid tumor or a solid tumor metastasis and said angiogenesis is tumor angiogenesis.

23. The method of claim 11 wherein said administering comprises intravenous, transdermal, intrasynovial, intramuscular, or oral administration.

24. The method of claim 22 wherein said administering is conducted in conjunction with chemotherapy.

25. The method of claim 11 wherein said administering comprises a single dose intravenously.

26. A method of inducing solid tumor tissue regression in a patient comprising administering to said patient a composition comprising a therapeutically effective amount of an integrin $\alpha_v\beta_5$ antagonist sufficient to inhibit neovascularization of a solid tumor tissue.

27. The method of claim 26 wherein said antagonist is a fusion protein, a polypeptide, a derivatized polypeptide, a cyclic polypeptide, a monoclonal antibody or an organic mimetic compound.

28. The method of claim 26 wherein said $\alpha_v\beta_5$ antagonist is the $\alpha_v\beta_5$ antagonist according to claim 6.

29. A method of inhibiting solid tumor tissue growth undergoing neovascularization in a patient comprising administering to said patient a composition comprising a therapeutically effective amount of an integrin $\alpha_v\beta_5$ antagonist sufficient to inhibit solid tumor tissue growth.

30. The method of claim 29 wherein said antagonist is a fusion protein, a polypeptide, a derivatized polypeptide, a cyclic polypeptide, a monoclonal antibody or an organic mimetic compound.

31. The method of claim 29 wherein said $\alpha_v\beta_3$ antagonist is the $\alpha_v\beta_3$ antagonist according to claim 6.

32. A method for treating a patient with inflammed tissue in which neovascularization is occurring comprising administering to said patient a composition comprising a therapeutically effective amount of an integrin $\alpha_v\beta_3$ antagonist.

33. The method of claim 32 wherein said antagonist is a fusion protein, a polypeptide, a derivatized polypeptide, a cyclic polypeptide, a monoclonal antibody or an organic mimetic compound.

34. The method of claim 32 wherein said $\alpha_v\beta_3$ antagonist is the $\alpha_v\beta_3$ antagonist according to claim 6.

35. A method for treating a patient in which neovascularization is occurring in retinal tissue comprising administering to said patient a composition comprising a neovascularization-inhibiting amount of an integrin $\alpha_v\beta_3$ antagonist.

36. The method of claim 35 wherein said antagonist is a fusion protein, a polypeptide, a derivatized polypeptide, a cyclic polypeptide, a monoclonal antibody or an organic mimetic compound.

37. The method of claim 35 wherein said $\alpha_v\beta_3$ antagonist is the $\alpha_v\beta_3$ antagonist according to claim 6.

38. A method for treating a patient for restenosis in a tissue wherein smooth muscle cell migration occurs following angioplasty comprising administering to said patient a composition comprising a therapeutically effective amount of an integrin $\alpha_v\beta_3$ antagonist.

39. The method of claim 38 wherein said antagonist is a fusion protein, a polypeptide, a derivatized polypeptide, a cyclic polypeptide, a monoclonal antibody or an organic mimetic compound.

40. The method of claim 38 wherein said $\alpha_v\beta_3$ antagonist is the $\alpha_v\beta_3$ antagonist according to claim 6.

41. A method of reducing blood supply to a tissue required to support new growth of said tissue in a patient comprising administering to said patient a composition comprising a therapeutically effective amount of an integrin $\alpha_v\beta_3$ antagonist sufficient to reduce said blood supply to said tissue.

42. The method of claim 41 wherein said antagonist is a fusion protein, a

polypeptide, a derivatized polypeptide, a cyclic polypeptide, a monoclonal antibody or an organic mimetic compound.

43. The method of claim 41 wherein said $\alpha_v\beta_5$ antagonist is the $\alpha_v\beta_5$ antagonist according to claim 6.

5 44. The method of claim 24 wherein said angiogenesis is present in a patient having an eye disease selected from the group of eye diseases consisting of diabetic retinopathy, age-related macular degeneration, presumed ocular histoplasmosis, retinopathy of prematurity and neovascular glaucoma.

10 45. The method of claim 24 wherein said angiogenesis is present in a patient having a corneal neovascular disorder selected from the group of disorders consisting of corneal transplantation, herpetic keratitis, luetic keratitis, pterygium and neovascular pannus associated with contact lens use.

46. The method of claim 24 wherein said angiogenesis is induced by a cytokine.

15 47. The method of claim 46 wherein said cytokine is selected from the group consisting of vascular endothelial growth factor, transforming growth factor- α and epidermal growth factor.

48. The method of claim 46 wherein said cytokine is vascular endothelial growth factor and said angiogenesis is selected from the group consisting of retinal angiogenesis, corneal angiogenesis, tumor angiogenesis and inflamed tissue angiogenesis.